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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	PAPER NUMBER
1652	12

DATE MAILED: 04/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/945,254	MEYERS ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-45 and 49-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-45 and 49-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 32-45, 49-56 are still at issue and are present for examination.

Applicants' amendments and arguments filed on 1-29-03, paper No.11, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

The disclosure is objected to because of the following informalities: The specification contains blank spaces in several pages (for example page 11, 12 etc.). Examiner urges the applicants to fill up those blank spaces with the appropriate information on the above pages and in all other pages where the blanks occurs in order to overcome this objection. Appropriate correction is required.

In response to previous Office action, applicants submit that they reserve the right to include ATCC deposit information when it becomes available and prior to issuance of the application. However, Examiner continues to object the specification until such time applicants provide the appropriate information.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 49-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 49-52 recite the phrase "detecting a labeled polypeptide or a labeled test compound". It is not clear to the Examiner as to how one skilled in the art can detect a labeled polypeptide or a labeled compound unless the polypeptide is labeled first or one uses a labeled compound. Amending the claim to recite the step of labeling prior to the step of "contacting" would overcome this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a compound which binds to a polypeptide comprising the amino acid sequence SEQ ID NO: 2, does not reasonably provide enablement for a method of identifying a compound which binds to a polypeptide comprising any contiguous 10 amino acids of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 42-45 are so broad as to encompass any human galactosyltransferase (HGT) comprising 10 consecutive amino acids of SEQ ID NO: 2. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of HGTs broadly encompassed by the claims including variants, mutants and recombinants. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single HGT.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any HGT which matches only to any 10 contiguous amino acids

with SEQ ID NO:2 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting HGT activity; (B) the general tolerance of human HGTs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any human HGT amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all or any human HGT with an enormous number of amino acid modifications of SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of binding agents that bind to any or all HGTs is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants traverse the above rejection arguing that the specification provides ample information regarding the structure/function relationship of the galactosyltransferase. Applicants go on to argue that they provide the various domains in figure 3 and 4 that are necessary for the activity. Applicants also argue that the specification describes extensively how to make and use fragments and drawn the attention of the Examiner to pages 26, 27 etc. and argue that they disclose various length fragments of the claimed polypeptides. While this may be so, none of the above description is required to be maintained within the HGT of the claims. At best the specification enables HGTs related to that of SEQ ID

NO:2 but not any HGT comprising just 10 consecutive amino acids of the same. Therefore, Examiner respectfully disagrees with such an argument to be persuasive to overcome the above rejection. Furthermore, a perusal of the specification does not provide a specific definition for "fragments" of polypeptides. Applicants do not make it clear that by reciting "fragments" they mean a sequence of amino acids of SEQ ID NO:2 which exhibits the claimed activity or what so ever. A perusal of page 26 and 27 of the specification indicates that applicants define in their terms what they mean by biologically active portion. There is no reference to the definition of "fragments". Applicants continue their argument that the specification teaches how to generate fragments of a polypeptide. However, such arguments are not persuasive to overcome the rejection as the claim continues to lack a structure/function relationship of the polypeptide. Applicants present arguments for the new claims in which they claim the use of a polypeptide that is 95% identical to SEQ ID NO:2 and has the galactosyltransferase activity. Such arguments are moot as Examiner has not included such claims in his rejection and does not present any arguments for overcoming the above rejection.

Claims 42-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 42-45 are directed to a method of identifying binding agents to polypeptide fragments (corresponding to 10 contiguous amino acid portions) of SEQ ID NO:2. Claims 42-45 are rejected under this section of 35 USC 112 because the claims are directed to a method

using a genus of polypeptide fragments of SEQ ID NO:2 that have not been disclosed in the specification. No description has been provided of the polypeptide fragment sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:2 has been provided by applicants, which would indicate that they had possession of the claimed genus of fragment polypeptides. The specification does not contain any disclosure of the function of all the polypeptide sequences derived from SEQ ID NO:2, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides, which can have a wide variety of functions (i.e., peptides which may have HGT-1 activity, high activity, low activity or no activity at all). Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicants traverse the above rejection mainly by quoting from the "Guidelines". While Examiner is fully aware of the facts and examples in the "Guidelines", contrary to applicants argument, Examiner would like to draw the attention of the applicants to the fact that the specification as written does not fully satisfy the requirements of 35 U.S.C. 112 first paragraph and contrary to the use of the argument from the "Guidelines"

that "it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by "other appropriate language" (see In re Grimme), in the instant application, it is necessary for the applicants to enumerate a plurality of species as the genus is not sufficiently identified in the application by "other appropriate language", i.e., there is neither a specific definition for fragments nor a disclosure of all the species in the genus "fragments". Applicants also take the example of RNA from the "Guidelines" and assert their position. However, Examiner respectfully disagrees with applicant's comparison as the present context is different from the situation in the example. Applicants present extensive arguments to support their amendment of other claims which is moot because Examiner has not rejected those claims. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus (i.e., a fragment which means either a single amino acid or two amino acids etc. may or may not have the desired activity of the polypeptide), one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or

features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera of claims 42-45 includes species which are widely variant in function. The genus of claims 42-45 is functionally diverse as it encompasses polypeptides with activity, those which lack such activity. As such, neither the description of the structure and function of SEQ ID NOS:2 nor the disclosure solely structural features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus. Hence the above rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32-45, 49-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conklin et al. (WO 01/44479 A1, filed on 12-15-2000 with a US priority date 12-16-1999 and GenSeq Accession No. AAE04752). Claims 32-45, 49-56 in this instant application are drawn to a method of identifying a compound which binds to a polypeptide comprising the amino acid with SEQ ID NO:2 wherein the method comprises either contacting a cell that expresses the polypeptide or the jus the polypeptide by itself with a test compound under conditions suitable for binding said polypeptide and determining whether said polypeptide binds to said test

compound by various methods as listed in the above claims. Conklin et al. teach the polypeptide with SEQ ID NO :2 (see enclosed sequence alignment), identify it as a galactosyltransferase homolog and assign various properties to the polypeptide and list its role in cell physiology. The reference also teaches that the polypeptide can be used to determine complementary molecules, agonists and antagonists, which are basically agents which binds and/or modulate the activity of the polypeptide (see page 6, 40-41). The reference also teaches that polypeptide may be used in methods that modulate cell-cell interactions, extracellular matrix interactions and glycoproteins modifications. While the reference does not explicitly teach an identical assay for identifying binding compounds for the polypeptide, using the teachings of the above reference and combining it with well established methods for assaying binding compounds existing in the art, it would have been obvious to one of ordinary skill in the art to use the polypeptide sequence which matches 100% with SEQ ID NO:2 of the instant application and develop methods for identification of compounds which bind to the polypeptide. One of ordinary skill in the art would have been motivated to do so as Conkliln et al. list the important roles played by the polypeptide. One of ordinary skill in the art would have a reasonable expectation of success since the above reference provides the polypeptide, characterizes it and lists its role in cell physiology and also suggests that binding compounds can be used for modulating the activity of the polypeptide.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

None of the claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Manjunath N. Rao Ph.D.
Patent Examiner, A.U. 1652
4/18/03